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Vascular Surgical Site Infection: Risk Factors and Preventive Measures

Dennis F. Bandyk, MD

Surgical-site infection (SSI) after arterial intervention is the most common nosocomial vascular infection and an important cause of postoperative morbidity. Its prevention requires the vascular surgeon to be cognizant of its changing epidemiology, patient risk factors, and effective measures to reduce its incidence. The majority of vascular SSIs are caused by Gram-positive bacteria, and methicillin-resistant *Staphylococcus aureus* has emerged as the prevalent pathogen, now involved in more than one-third of cases. Nasal carriage of methicillin-sensitive or methicillin-resistant *S. aureus* strains, recent hospitalization, failed arterial reconstruction, and presence of a groin incision, are major risk factors for developing vascular SSI. Overall, the vascular SSI rate is higher than predicted by Center for Disease Control National Nosocomial Infections Surveillance risk category system, and ranges from 1% to 2% after open or endovascular aortic interventions to as high as 10% to 20% after lower-limb bypass grafting procedures. Use of preoperative measures to reduce *S. aureus* nasal and skin colonization in conjunction with appropriate, bactericidal antibiotic prophylaxis, meticulous wound closure, and postoperative care to optimize patient host defense regulation mechanisms (temperature, oxygenation, blood sugar) can minimize SSI occurrence.
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VASCULAR SURGICAL-SITE infection (SSI) occurs as a result of perioperative events leading to bacterial colonization of the wound and frequently the underlying prosthetic graft, when present. Patients undergoing arterial interventions are at increased risk for SSIs, with an overall incidence in the range of 5% to 10%—significantly higher than the 2% to 6% rate predicted by Centers for Disease National Nosocomial Infections Surveillance System for "clean" procedures in risk index categories 1 and 2.[1] The greater likelihood of SSI occurrence in the vascular surgery patient is due to both procedure- and patient-specific risk factors. Implantation of a vascular prosthesis increases SSI risk by producing a microenvironment conducive for bacterial attachment and biofilm formation, which sustains bacterial colonization and protects encased organisms from host defenses and antimicrobial therapy. Injured skin/skin structures and soft tissue edema, common sequelae following femoral and lower-limb arterial revascularizations, impede wound healing. Incisions with skin separation, underlying hematoma, and serous wound drainage extend the time available for bacteria invasion from external sources, bacteremia, or via bacteria transport to the wound via lymphatic channels. A nonhealing wound facilitates bacterial invasion and, if not addressed promptly, can progress to an SSI, with its attendant increased morbidity and health care costs from an extended length of hospitalization, returns to the operating room for wound debridement/closure procedures, home health care, and outpatient visits for wound management. Prevention of SSI is a paramount concern for vascular surgeons, and reducing the incidence requires knowledge of its changing epidemiology, risk factors for development, and use of effective patient-care strategies.

Infection involving a vascular wound may be superficial, ie, cellulitis, deep incision involving the subcutaneous tissue/fascia, or involving other areas than the incision itself, ie, organ/space, such as along the length of an implanted vascular prosthesis or as an intracavitary aortic graft infection. For autogenous arterial revascularizations, only infections occurring within 30 days should be classified at an SSI, but when a prosthetic graft or endovascular device is implanted the incidence of SSI is calculated for 1 year, not for only 30 days following the procedure. The diagnostic criteria for SSI should include signs/symptoms of infection (pain, tenderness, erythema, swelling), purulent drainage from the wound,

Division of Vascular and Endovascular Surgery, University of South Florida College of Medicine, Tampa, FL.

Address reprint requests to: Dennis Bandyk, Division of Vascular and Endovascular Surgery, USF Health South, 7th Floor, 2A Columbia Drive, Tampa, FL 33606. E-mail: dbandyk@health.usf.edu

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and organisms isolated from aseptically obtained cultures of fluid or tissue.

Changing Epidemiology of Vascular SSI

Although virtually any microorganism can produce an SSI or infect a vascular prosthesis, Gram-positive bacteria, especially *Staphylococcus aureus*, are the prevalent pathogens involved in approximately 80% of all cases.[2-5] As in other surgical disciplines, the microbiology of vascular SSIs has changed in the past decade, with increased prevalence of antibiotic-resistant organisms, including staphylococcal strains. An audit of prosthetic arterial graft infections treated by our vascular surgery group demonstrated a fourfold increase in methicillin-resistant *S. aureus* (MRSA) infection from 10% in the 1990s to 40% since 2000. In a series of complex vascular SSIs treated by aggressive staged surgical debridement, antibiotic bead therapy, and selective sartorius muscle flap coverage, MRSA accounted for 20% of all infections and 50% of reinfections.[2] This trend has been verified from other vascular centers in the United States and Europe. A 2005 report from the University of Texas Galveston vascular group reported an SSI rate of 11% after lower-extremity bypass grafting with *S. aureus* involved in 64% of cases, of which one-half were caused by MRSA.[5] Today, MRSA should be suspected in any vascular patient presenting with a SSI, including patients with a nonhealing lower-limb amputation performed for ischemia. The changing microbiology of SSIs, especially the dramatic increase in MRSA infection, has implications for both initial treatment of SSIs, as well as antibiotic prophylaxis in vascular patients with multiple risk factors for postoperative infection. Patient outcomes are less favorable with a MRSA SSI compared to methicillin-sensitive *S. aureus* (MSSA) infection, with an increase in both 30-day mortality (odds ratio of 3.4) and morbidity (median of five additional hospitalizations).

The appearance time for vascular SSIs depends on procedure type and whether a prosthetic graft has been implanted. Although wound infections typically manifest clinically within 30 days, infection involving a lower-limb prosthetic arterial bypass usually presents beyond 4 months (mean = 7 months); and after aortic grafting, clinical signs of infection may appear years later (mean = 3.5 years).[2] Late presentation of vascular graft infection can be attributed to the bacteria biofilm nature of the infectious process and the low virulence of infecting bacteria—most commonly *S. epidermidis*. With time, graft biofilm infection can evolve to a more virulent infectious process with superinfection by other bacteria, such as MSSA or MRSA, especially if graft cutaneous sinus tract develops. If the presentation of aortic graft infection includes Gram-negative bacteremia, graft enteric erosion should be suspected. Overall, Gram-negative bacteria account for approximately 20% to 25% of vascular SSI, with the most common strains being *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus* sp., and *Klebsiella pneumonia*. When confronted with a vascular SSI, initial antibiotic therapy should be guided by Gram's stain of wound or perigraft fluid. Identification of Gram-positive organisms should prompt antibiotic therapy with bactericidal killing properties to MRSA.[6]

Risk Factors for Vascular SSI

The majority of arterial surgery procedures are classified as "clean" Class I by the National Research Council because the operative exposure and revascularization is performed in uninfected tissues without inflammation; the respiratory, alimentary, or infected urinary tract is not entered; and the wound is closed primarily with suction drainage if necessary.[1] Although diseased arteries can harbor bacteria, most commonly *S. epidermidis* strains, within atherosclerotic plaque or mural thrombus; the inoculum and virulence are considered low. However, this observation is an important rationale for routine antibiotic prophylaxis. Arterial revascularization is not recommended in patients with invasive remote infection or bacteremia, except when the intervention is judged life-saving, or for treatment of a mycotic aneurysm. In patients with critical limb ischemia and a clinical presentation of foot sepsis or wet gangrene, initial management should be surgical debridement of infected tissues in conjunction with antibiotic therapy; followed by open or endovascular revascularization when the invasive infectious process has been controlled.

Whether an SSI develops involves a complex interaction between a bacteria inoculum, host defense mechanisms, and surgical site healing. Audits performed in US hospitals of SSIs have identified patient-, procedure-, and environmental-related risk factors that increase the risk for postoperative infection (Table 1). For the vascular patient, the most significant risk factors are nasal colonization with MSSA/MRSA, presence of a groin incision, prosthetic grafting or patch angioplasty, lower-limb arterial bypass grafting, postoperative bacteremia, and end-stage renal disease. Characteristics such as obesity, advanced age, smoking, and diabetes shown to be risk factors for SSI are also present in many vascular patients.

Numerous studies have confirmed increased SSI rates in persons with *S. aureus* nasal carriage. Approximately 10% to 35% of healthy persons persistently carry *S. aureus* in their nares with the prevalence increasing in patients with end-stage renal disease, active skin infection, immune deficiency states such as infection with human immunodeficiency virus, or residence in a long-term care facility. Preoperative *S. aureus* carriage has been shown to increase the risk of SSI by four- to eightfold in patients undergoing cardiothoracic, neurosurgical, and orthopedic procedures. The "cause-and-effect" mechanism is felt to be patient transmission of bacteria from the nares to the surgical site(s) via their hands. Nasal colonization with MRSA versus MSSA further increases the likelihood of SSI to approximately 8- to 10-fold compared to a *S. aureus* carrier, and has been linked to with MRSA SSI outbreaks in hospital wards. In vascular patients, MRSA colonization has been shown to increase frequency of any nosocomial (wound, blood, urine, lung) infection (44% incidence and odds ratio of 4.5) and, in patients who develop a MRSA infection, hospital stay was prolonged. These epide-

Table 1 Patient, Procedure, and Environmental Risk Factors for Surgical Site Infection

Patient-related risk factors
Nasal carriage of *Staphylococcus aureus*
Prolonged preoperative length of stay
Postoperative bacteremia
End-stage renal disease
Obesity
Malnutrition/low serum albumin
Older age
Smoking/nicotine use
Diabetes mellitus
Prior incision site irradiation
Malnutrition/low serum albumin
Autoimmune disease/corticosteroid therapy
Malignancy/chemotherapy
Procedure-related risk factors
Femoral/groin incision
Remote infection
Biomaterial implant
Emergency/preoperative procedure
American Society of Anesthesiology score >2
Extended operative time
Hypothermia
Shock
Hyperglycemia
Environmental risk factors
Operating suite ventilation—environmental surface cleaning
Instrument and vascular implant sterility
Surgical attire and sterile operative technique

miologic observations prompted a randomized clinical trial of decolonizing therapy with application of intranasal antibiotic ointment (mupirocin calcium) prior to and following surgical procedures.[4] Mupirocin, a topical antistaphylococcal agent that inhibits RNA and protein synthesis, eliminated *S. aureus* carriage in 83% of colonized patients (23% of study population) compared to no effect in the placebo group. Of note, this study demonstrated the odds of an *S. aureus* carrier developing SSI was 4.5 times that of a noncarrier ($P < .001$). Although there was a trend to reduced *S. aureus* SSIs (38% reduction) the differences between the treatment and placebo groups was not significant (7.9% *v* 8.5%). These data confirm an increased SSI risk in MSSA and MRSA nasal carriers, but reduction in postoperative infection rate requires a treatment strategy beyond intranasal decolonization alone. Further, prolonged use of topical mupirocin has been associated with development of resistant strains. An audit of patients admitted to our vascular service for elective arterial intervention demonstrated an overall 8% incidence of MRSA nasal colonization, but 40% in end-stage renal disease patient population. Risk factors for MRSA colonization/infection mirror those of nasal *S. aureus* colonization (Table 2).[7] A recent report from Switzerland indicated a policy of universal screening of surgical patients for MRSA prior to admission and nares decolonization in carriers may not decrease nosocomial infection.[8] To produce a significant decrease in SSI infection, specific surgical site care and antibiotic prophylaxis care directed at antibiotic-resistant bacteria is necessary.

Procedure-specific risk factors for vascular SSI include "open" versus endovascular intervention, presence of a femoral groin incision, and prosthetic graft/patch usage. If a procedure lasts >3 hours, produces shock or hypothermia, or requires blood transfusion, the likelihood of postoperative infection is increased. Intraoperative hypothermia of 1°C to 1.5°C increases the relative risk of postoperative infection twofold. SSI is lowest after abdominal aortic aneurysm repair, with a similar incidence following open (0.2%) and stent-graft (0.16%) repair and increased in patients who developed any nosocomial infection during hospitalization.[7] Similarly, carotid endarterectomy and endovascular interventions involving stent-angioplasty (carotid, visceral, iliac, femoropopliteal) also are associated with low (<1%) SSI rate. By contrast, open arterial reconstructions for peripheral arterial disease are associated with overall wound and graft infection rates of 8% to 10%—significantly higher following infrainguinal prosthetic (10%-29%) or in situ saphenous vein (18%-22%) bypass grafting procedures.[5,9,10] The increased SSI of lower-limb arterial procedures is related to tissue injury of critical ischemia, secondary lymphedema produced by surgical trauma and revascularization edema, and failure of the femoral/groin incision to heal. Development of wound hematoma or incision separation caused by dermal or underlying fat necrosis reduces the bacteria inoculum required to produce an invasive infection. These wound problems occur more frequently in the groin, especially in the clinical setting of a redo arterial construction or an obese, diabetic patient. Extensive application of electrocautery and extended application of wound retractors can produce skin and soft tissue trauma and results in a large volume of necrotic tissue evident on the first postoperative day by cyanotic incision skin margins. Any condition that impairs primary wound healing increases the likelihood of SSI. This includes failure of prosthetic graft healing by incorporation by surrounding soft tissue. The finding by duplex scanning of perigraft fluid after polytetrafluoroethylene or polyester arterial bypass grafting beyond 3 to 4 months after operation is abnormal and sus-

Table 2 Risk Factors for Methicillin-Resistant *Staphylococcus Aureus* Infection

Known previous MRSA infection
Immunosuppression
Diabetes mellitus type I
Chronic open wounds
Previous antibiotic use within 90 days
Central venous catheterization
Residence in a long-term facility
Prolonged hospitalization
ICU admission
Dialysis
Advanced age
Hospitalization before onset of infection

Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*.

picious for a low-grade graft infection especially if associated with local signs of inflammation.

Preventive Measures

A multipronged approach is required to minimize the occurrence of vascular SSI, including attention to pre-, intra-, and postoperative preventive measures published by the Centers for Disease Control in 1999 (www.cdc.gov/ncidod/dhqp/gl_surgicalsite.html).[11,12] The guidelines address aspects of patient preparation, sterile surgical technique, surgical team antisepsis, hand disinfection, incision care, and antimicrobial prophylaxis. Surveillance of patients for nasal carriage of *S. aureus*, especially MRSA, as well as a review in each patient of the inventory of SSI risk factors, can identify the "high-risk" cases and prompt an individualized prevention strategy. The increasing incidence of drug-resistant Gram-positive infections after arterial surgery is a concern and serves to reemphasize the importance of preventive strategies. Surgeons should recognize that expanding the coverage of antibiotic prophylaxis is not a primary solution. Instead prevention strategies to decolonize the *S. aureus* carrier in combination with meticulous wound care and thoughtful antibiotic prophylaxis is recommended. There is accumulating evidence that regulation of host defense factors—body temperature, oxygenation, and blood sugar—are important in determining the SSI risk in an individual patient. Care measures to maintain normal temperature during and after surgical procedures, use of insulin therapy to keep blood sugar levels <180 mg/dL, and pulse oximetry monitoring to ensure 100% hemoglobin saturation are associated with reductions in SSI rates. Supplemental oxygen in the immediate postoperative period improves incisional oxygen tension and decreases wound healing complications.[11]

Antimicrobial prophylaxis in vascular patients should include therapy directed at *S. aureus* nasal colonization, parenteral antibiotic therapy to assure adequate tissue levels are achieved before the procedure is begun and throughout the procedure, and surgical site care to impede bacterial colonization of injured skin and soft tissue (Table 3).[11,12] For effective antibiotic prophylaxis, a first- or second-generation cephalosporin alone or in conjunction with daptomycin should be administered 30 to 60 minutes prior to the procedure. Prophylaxis must be provided for both Gram-positive and Gram-negative bacteria. Use of daptomycin or vancomycin alone is not recommended. When vancomycin is used for prophylaxis, the drug should be administered 60 to 120 minutes prior to incision because drug distribution to tissues and bacteriocidal activity is achieved more slowly. Cephalosporin antibiotics should be redosed if the procedure takes longer than 3 hours or if blood loss exceeds 1.5 L. If the patient is allergic to cephalosporins, aztreonam is an appropriate substitute. Antibiotic therapy is recommended for 24 hours.

Daptomycin is a concentration-dependent, bactericidal cyclic lipopeptide antibiotic with activity against all Gram-positive bacteria, including MRSA, penicillin-resistant streptococci, and vancomycin-resistant enterococci. Its once-daily dosing, rapidly bactericidal activity within 30 minutes after intravenous administration and prolonged (18 to 24 hour) postantibiotic effect make it particularly convenient and attractive for prophylaxis therapy. Daptomycin cannot be used

Table 3 Treatment Strategies to Prevent Vascular Surgical Site Infection

Surveillance
Patient screening for nasal carriage of *Staphylococcus aureus*, including MRSA
Decolonization
Preoperative intranasal mupirocin (applied to both nares for 3 days prior and 2 days after operation)
Hibiclens (4% chlorhexidine gluconate) wipes or body washing at planned incision site to decolonize skin surfaces for 3 days prior to procedure
Antibiotic prophylaxis
Low risk: carotid endarterectomy, percutaneous endovascular stent/stent-angioplasty
Cefazolin, weight-based, 1 to 3 g IV slowly 60 min prior to procedure, and repeated 1-2 g if procedure >3 h or blood loss >1.5 L. Dosing repeated every 8 hours for 24 hours; or cefuroxime 1.5 g IV 60 min prior to surgery and every 12 hours for total of 6 g.
If patient has a cephalosporin allergy, give aztreonam 1 g IV 60 min prior to procedure and every 8 hours for 24 hours
High risk: groin incision, prosthetic grafting, dialysis access procedures, lower-extremity bypass grafting, *S. aureus* nasal carriage, history of MRSA infection, multiple risk factors
Add daptomycin 6 mg/kg (single dose) IV slowly 60 min prior to procedure; a second choice but not preferred, vancomycin 1 g IV slowly over 1 h 60-120 minutes prior to the procedure.
Antibiotic-impregnated prosthetic graft
Soak gelatin-coated polyester or polytetrafluoroethylene vascular prosthesis in a rifampin (30-60 mg/mL) solution for 15 min
Incision care
Femoral/groin incision: Apply silver-impregnated wound dressing (Acticoat) for 24-48 h; followed by topical mupirocin ointment to incision if wound drainage or injured skin edges present.
Apply sterile dressing daily for 48 h
Wash hands before and after dressing changes
Educate patient and family regarding surgical site care, and symptoms of SSI

Abbreviations: IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*.

alone for vascular procedure prophylaxis because it does not have activity for Gram-negative bacteria known to produce vascular SSIs. In the MRSA-colonized patient requiring lower-limb prosthetic bypass graft, ie, a "high SSI risk procedure," our vascular group has continued daptomycin prophylaxis for a total of 48 hours (two doses).

A policy of universal screening for MRSA colonization should be considered in all vascular patients considered to be at risk for SSI based on patient- or procedure-specific characteristics.[12,13] A nasal swab of both nares should be submitted for polymerase chain reaction identification of bacteria. Results are typically available within several hours and testing is reimbursed by Centers of Medicare and Medicaid Services. If screening is not possible, all patients should receive a prescription for mupirocin nasal ointment and chlorhexidine antiseptic skin cleanser for use 3 days prior to an elective arterial revascularization procedure. Daily preoperative skin cleansing with chlorhexidine produces a persistent antibacterial effect at the incision site after operation.

The importance of postoperative wound care cannot be overemphasized. Silver-coated wound dressings should be applied to groin incisions in the operating room and not disturbed for 24 to 48 hours unless wound drainage occurs. All dressing changes should be performed using sterile technique with hand washing prior to and after wound care is provided. If incision edges are traumatized, mupirocin ointment should be applied to produce an antibacterial barrier. If the surgical site demonstrates skin-edge necrosis, hematoma, or profuse lymphatic drainage with surrounding tissue edema, a more aggressive wound management strategy is required. This may consist of operative exploration of the wound, antibiotic irrigation, closure suction drainage, and a secure skin-closure technique.

Summary

Antimicrobial-resistant pathogens are increasing involved in vascular SSI. A program of patient surveillance for nasal carriage for MRSA, nasal and skin decolonization, preventing transmission to other patients, and thoughtful antibiotic prophylaxis usage is an effective strategy to reduce SSI. The entire surgical team must participate in institutional efforts to control nosocomial infections, antimicrobial resistance in bacteria, and SSI rates.

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